



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Patient Health Protection

Guidelines on good pharmacovigilance practices (GVP)

Introductory cover note to the public consultation of the first seven modules

Background to public consultation on GVP

New legislation for pharmacovigilance will apply in the European Union (EU) as of July 2012, and to support its implementation a new set of guidelines for the conduct of pharmacovigilance in the EU is under development which, as they are adopted, will replace the current set in Volume 9A of the Rules Governing Medicinal Products in the EU.

This new guidance on good pharmacovigilance practices (GVP) is organised into Modules, and the first seven Modules on prioritised topics are now available for public consultation.

Objectives of pharmacovigilance

Pharmacovigilance has been defined by the World Health Organization (WHO) as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem.

In line with this general definition, underlying objectives of the applicable EU legislation for pharmacovigilance are:

- preventing harm from adverse reactions in humans arising from the use of authorised medicinal products within or outside the terms of marketing authorisation or from occupational exposure; and
- promoting the safe and effective use of medicinal products, in particular through providing timely information about the safety of medicinal products to patients, healthcare professionals and the public.

Pharmacovigilance is therefore an activity contributing to the protection of patients' and public health.

Pharmacovigilance in the EU: roles of different actors

In the EU, a regulatory network, consisting of the competent authorities in Member States, the European Commission and the European Medicines Agency (in GVP referred to as "the Agency") is responsible for granting marketing authorisations and supervising medicinal products, including the



conduct of pharmacovigilance. The Agency has a core role in coordinating these activities for the network.

In addition to the network's responsibilities, EU legislation imposes responsibility for pharmacovigilance, together with specific obligations (i.e. in terms of tasks and responsibilities), on marketing authorisation holders.

In the past the role of healthcare professionals was mainly seen as contributing to pharmacovigilance through spontaneous reporting of suspected adverse reaction cases and as receiving, together with the patients, advice on minimising risks through updated product information or other information materials. However over time, participation of patients and healthcare professionals in EU regulatory processes, including those for pharmacovigilance, has steadily increased. A large number of Member States have established, over the last years, schemes for reporting of suspected adverse reactions by patients themselves. An EU legal framework for patient reporting in all Member States has now been introduced through the new pharmacovigilance legislation. The new legislation further increases public participation by including patient and healthcare professional representatives in the new Pharmacovigilance and Risk Assessment Committee (PRAC) and through public hearings on pharmacovigilance and benefit-risk matters at the Agency, involving all stakeholders.

Legal basis, scope and process for GVP

The legal framework for pharmacovigilance of medicinal products for human use in the EU is given in Regulation (EC) No 726/2004 and Directive 2001/83/EC on the Community code relating to medicinal products for human use, as amended in 2010 by Regulation (EU) No 1235/2010 and Directive 2010/84/EU respectively, as well as by the Commission Implementing Regulation on the Performance of Pharmacovigilance Activities Provided for in Regulation (EC) No 726/2004 and Directive 2001/83/EC (at the time of this consultation available in draft only). It should be noted that Chapter 3 of the Regulation (EC) No 726/2004 as amended, Title IX of the Directive 2001/83/EC as amended and the draft Implementing Regulation contain the majority of pharmacovigilance provisions in the legislation, however, other measures directly relevant to the conduct of pharmacovigilance are found in other Chapters and Titles of this Regulation and Directive.

The aforementioned amending legislation of 2010, together with the related draft Implementing Regulation, is commonly referred to as the new pharmacovigilance legislation in the EU. It was the outcome of a major review of the current pharmacovigilance system in the EU conducted by the European Commission, followed by a formal law-making process in the Council and European Parliament. The legislation has the primary aim to strengthen and rationalise pharmacovigilance and increase patient safety.

The pharmacovigilance legal requirements and GVP apply to all medicinal products authorised in the EU, whether centrally or nationally authorised. While risk proportionality underpins the new legislation, the requirements are generally the same for different types of product unless specific provision or exemptions apply as indicated in the GVP Modules.

GVP is drawn up to facilitate the performance of pharmacovigilance activities within the EU and applies to marketing authorisation holders in the EU, the Agency and competent authorities in Member States. Iceland, Liechtenstein and Norway have so far, through the Agreement of the European Economic Area (EEA), adopted the complete Union *acquis* (i.e. the legislation at EU level, guidelines and judgements) on medicinal products, and are consequently parties to the EU procedures. The new pharmacovigilance Regulation (EU) No 1235/2010 and Directive 2010/84/EU will however only formally apply to these countries once they have been incorporated into the EEA Agreement. In the meantime and thereafter,

where in GVP reference is made to Member States of the EU, this should be read to include Norway, Iceland and Liechtenstein¹.

GVP is drawn up based on Article 108a of Directive 2001/83/EC as amended, by the Agency in cooperation with competent authorities in Member States and interested parties.

GVP is being developed within a governance structure set up by the Agency and national competent authorities specifically for the implementation of the new pharmacovigilance legislation. This structure allows for the close collaboration of Member States, the Agency and the European Commission services, with regular stakeholder meetings an integral part of the implementation process.

Each draft Module of GVP has been prepared by a project team consisting of experts from Member States and the Agency, taking into account comments collected during the stakeholder meetings. The draft Modules were agreed by the Heads of Medicines Agencies' European Risk Management Strategy Facilitation Group (ERMS FG) and are released on behalf of the EU regulatory network.

After public consultation, the Modules will be finalised within the governance structure, addressing the comments from stakeholders, and then published by the Agency.

Referencing of legal requirements in GVP

In GVP, any reference to Regulation (EC) No 726/2004 and Directive 2001/83/EC refers to the Regulation and Directive respectively, always including their latest amendments. Where reference is made to specific Articles in square brackets "REG" means Regulation (EC) No 726/2004 as amended and "DIR" means Directive 2001/83/EC as amended. If reference is provided to any other Regulation or Directive, its full reference is provided.

Reference to specific Articles of the draft Commission Implementing Regulation on the Performance of Pharmacovigilance Activities Provided for in Regulation (EC) No 726/2004 and Directive 2001/83/EC is provided in square brackets with the indication "IM". As this Implementing Regulation has not yet been finalised, references to its articles in the draft GVP Modules is for illustrative purposes only.

Text in GVP describing legal requirements makes reference to the specific article in the legislation and uses the same modal verb as used in the article, which is usually "shall". Guidance for the implementation of legal requirements is presented with the modal verb "should".

Structure of GVP

Pharmacovigilance activities are organised by distinct but connected processes, and each GVP Module presents one major pharmacovigilance process.

A draft list of current draft and envisaged GVP Modules (see Annex 1) identifies the prioritised Modules subject to this public consultation in bold font type. The other envisaged Modules are currently under development and will be subject of future public consultations. Currently some guidelines dedicated to product- or population-specific aspects of pharmacovigilance are published on the Agency's website. They remain valid in principle (unless any aspect is not compatible with the new legislation) until they are revised at a later point in time for inclusion in GVP.

Within the Modules, Sections A provide the legal, technical and scientific context of the respective process. Sections B give guidance which, while based on EU legislation, reflects scientific and regulatory approaches, formats and standards agreed internationally in various fora, or where such

¹ The only exemption from this is that legally binding acts from the EU (e.g. Commission Decisions) do not directly confer rights and obligations but have first to be transposed into legally binding acts in Norway, Iceland and Liechtenstein.

formal agreements or expert consensus does not exist, Sections B describe approaches which are considered in line with general current thinking in the field. Sections C focus on the specifics of applying the approaches, formats and standards in the EU and other aspects of operating the respective process in the EU.

In particular in Sections B, the term “competent authority” is to be understood in its generic meaning of an authority regulating medicinal products and/or an authority appointed at national level for being in charge of all or individual pharmacovigilance processes. For the purpose of applying GVP in the EU, the term “competent authority” covers the competent authorities in Member States and the Agency.

Practical advice for the public consultation

Those participating in the public consultation are asked to please submit comments by using the specific templates for each Module (see page 1 of each draft Module) and the Definition Annex. An additional template for general comments is provided [here](#). Comments will only be processed if submitted as **completed templates in open word format**. Participants may additionally submit pdf files of their comments if they wish to do so if they accompany them by a statement that the open and pdf files are identical in content.

The deadline for submitting comments is **18 April 2012**.

The public consultation relates to the guidance proposed for the practical implementation of the applicable legislation. Participants are therefore asked not to comment on the underlying legal requirements (identified in the draft Modules by reference to the respective Articles), as these cannot be altered through the GVP consultation process.

Participants should note that their comments will be published on the Agency’s website, identifying the sender’s organisation (but not the sender’s name). Where a sender does not represent an organisation but submits comments as an individual, the sender’s name will be published unless the sender objects against the publication. In the absence of a legitimate interest to oppose the publication of the name, the contribution will not be published nor will, in principle, its content be taken into account. Please consult the Agency’s Privacy Policy

(http://www.ema.europa.eu/ema/index.jsp?curl=pages/home/general/general_content_000516.jsp&mid) and the specific privacy statement for this consultation

(http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/02/WC500123144.pdf).

Specific question on transition to new requirements

In addition to commenting on any section of GVP Modules (using the specific templates for each Module), those participating in the public consultation are specifically asked to consider the question below and provide comments in the comments template for the respective Module they are referring to:

The European Commission recently published a Question and Answers document on transitional arrangements concerning the entering into force of the new legal requirements (see http://ec.europa.eu/health/files/pharmacovigilance/2012_02_qa_phv.pdf). In the GVP consultation responses, stakeholders are asked to highlight any areas where you think additional guidance on interim arrangements is required.

Timelines for finalisation of GVP

The draft Modules subject to this public consultation are envisaged to be finalised and published by July 2012. Drafts of further Modules will be released for public consultation in the course of 2012.

The European Medicines Agency thanks all those participating in the public consultation for their contributions.

Annex: Draft list of GVP Modules²

GUIDANCE ON GOOD PHARMACOVIGILANCE PRACTICES (GVP)

INTRODUCTION	Legal Basis and Structure of Pharmacovigilance Guidance
MODULE I	Pharmacovigilance Systems and their Quality Systems
MODULE II	Pharmacovigilance System Master File
MODULE III	Pharmacovigilance Inspections
MODULE IV	Audits
MODULE V	Risk Management Systems
MODULE VI	Management and Reporting of Adverse Reactions to Medicinal Products
MODULE VII	Periodic Safety Update Reports
MODULE VIII	Post-Authorisation Safety Studies
MODULE IX	Signal Management
MODULE X	Additional Monitoring
MODULE XI	Public Participation in Pharmacovigilance
MODULE XII	Continuous Pharmacovigilance, Ongoing Benefit-Risk Evaluation, Regulatory Action and Planning of Public Communication
MODULE XIII	Incident Management
MODULE XIV	Referral Procedures for Safety Reasons
MODULE XV	Safety Communication
MODULE XVI	Tools, Educational Materials and Effectiveness Measurement for Risk Minimisation

PRODUCT- AND POPULATION-SPECIFIC CONSIDERATIONS

ANNEX I	DEFINITIONS
ANNEX II	TERMINOLOGY
ANNEX III	TEMPLATES
ANNEX IV	LIST OF INTERNATIONAL PHARMACOVIGILANCE GUIDANCE DOCUMENTS
ANNEX V	LIST OF OTHER GUIDANCE DOCUMENTS

² Modules in bold font type are included in the first round of public consultation launched in February 2012.